



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,941	10/08/2004	Jens Tonne Andersen	10297.204-US	1508
25908 7590 09/25/2007 NOVOZYMES NORTH AMERICA, INC. 500 FIFTH AVENUE SUITE 1600 NEW YORK, NY 10110			EXAMINER ROBINSON, HOPE A	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 09/25/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/510,941

Applicant(s)

ANDERSEN ET AL.

Examiner

Hope A. Robinson

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-62 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41-62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/22/07</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Notice to Comply</u> . |

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed July 28, 2006, on January 22, 2007 is acknowledged.

Claim Disposition

2. Claims 41-62 are pending and are under examination.
3. The following objections and rejections are or remain applicable.

Sequence Compliance

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicant is required to identify all amino acid sequences of at least 4 L-amino acids and at least 10 nucleotides by a sequence identifier, i.e., "SEQ ID NO:". It is noted that applicant filed a CFR and Sequence listing on October 8, 2004, however the sequence erred which is outlined on the error report. If these sequences have not been disclosed in the computer readable form of the sequence listing and the paper

Art Unit: 1652

copy thereof, applicant must provide a computer readable form of the "Sequence Listing" including these sequences, a paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and computer readable form copies are the same and, where applicable, include no new matter as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See the attached Notice to Comply with the sequence rules and error report.

Claim Objection

5. Claims 41, 48 and 54-55 are objected to because of the following informalities:

For clarity and precision of claim language it is suggested that the phrase "identical host cell" is deleted from the claim and instead replaced with "the parent *Bacillus licheniformis* host cell", because it is unclear what constitutes "identical", if it is based on function, sequence or some other parameter.

For clarity and precision of claim language it is suggested that claim 48 is amended to read "The host cell of claim 43, wherein the heterologous gene(s) are in an operon".

For clarity and precision of claim language it is suggested that claim 54 is amended to read, "The host cell of claim 53, wherein the enzymes are selected from the group consisting of oxidoreductases (EC1), transferases (EC2)....":

Art Unit: 1652

For clarity it is suggested that claim 55 is amended to read, "The host cell of claim 53, wherein the enzymes have an activity selected from the group consisting of aminopeptidase..."

Correction is required.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 41-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making proteins in a host cell, does not enable a method to produce any products or the genus of heterologous proteins/genes encompassed in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does

Art Unit: 1652

not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)). The factors most relevant to the instant invention are discussed below.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states that, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art". "The amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled.

The claimed invention is directed to a "A *Bacillus licheniformis* mutant host cell, said mutant host cell is derived from a parent *Bacillus licheniformis* which mutant host

Art Unit: 1652

cell comprises a mutation in a gene encoding a polypeptide involved in antibiotic synthesis, wherein said gene is native to said host cell, and wherein said gene encodes a polypeptide which is at least 95% identical to the polypeptide of SEQ ID NO:2", however, the instant specification does not provide support for the claims as they are broadly drawn and encompass an unspecified amount of heterologous genes and polypeptides. In addition, the claims broadly read on any polypeptide involved in antibiotic synthesis and the instant specification does not clearly define "how involved".

The quantity of experimentation necessary would be undue as the claims encompass an unspecified amount of heterologous genes and proteins. Furthermore, no reasonable correlation is made between function and structure. Additionally, the claims recite that genes are either partially or completely deleted to produce the claimed mutant host cell, however, there is no indication of what genes. . For instance the art demonstrated via precise deletions in tagB, tagF and tarD, a disturbance in the teichoic acids found in the wall of the gram-positive bacteria *Bacillus subtilis* based on gene deletions (see, Bhavsar et al., Journal of Bacteriology, December 2004, vol. 186, no. 23, pages 7865-7873). As the art supports the unpredictability of structural modifications, a correlation between structure and function is critical in view of the mutations contemplated in the instant application in a similar organism to a greater extent. Further the claims recite the open language of "comprising" thus there is no limit on how many genes can be completely deleted, no limit on the percentage of how much polypeptides are expressed in a lesser amount based on said mutation, no limit on the number of heterologous genes or polypeptides. Moreover the claims to the recited

Art Unit: 1652

process are unlimited with respect to what "product of interest" is used. It is noted that the instant specification discloses a protein product, however, the claims read on any product, which is not supported by the disclosure. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. Therefore, for all these reasons the claimed invention is not enabled and specification is not commensurate in scope with the claims.

7. Claims 41-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a " A *Bacillus licheniformis* mutant host cell, said mutant host cell is derived from a parent *Bacillus licheniformis* which mutant host cell comprises a mutation in a gene encoding a polypeptide involved in antibiotic synthesis, wherein said gene is native to said host cell, and wherein said gene encodes a polypeptide which is at least 95% identical to the polypeptide of SEQ ID NO:2", however, the instant specification does not provide adequate written description because the claims encompass an unspecified amount of heterologous genes and polypeptides. In addition, the claims broadly read on any polypeptide involved in antibiotic synthesis and the instant specification does not clearly define "how involved". The specification provides no information on the function of a polypeptide whose

Art Unit: 1652

sequence is disclosed in SEQ ID NO:2, other than the involvement in antibiotic synthesis, or any particular region or amino acids thereof which have any significance to this function of the polypeptide or identified any conserved regions/domains. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one skilled in the art cannot envision all the mutant host cells having mutations in genes encoding polypeptides which are involved in "antibiotic synthesis", for example. The specification provides no information regarding the precise amino acids, or even which general regions of the polypeptide whose sequence is shown in SEQ ID NO:2, can be altered, and remain involved in antibiotic synthesis. There is no structure-function analysis of the disclosed polypeptide shown in SEQ ID NO:2 that could be modified and retain function in antibiotic synthesis. Thus, the claimed invention is directed to a large variable genus, for which the specification fails to provide any additional representative species of the claimed genus, to show that applicant was in possession of the claimed genus.

A representative number of species means that the species, which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of

Art Unit: 1652

such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Further, *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993).

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 41-62 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 41 is confusing, the claim recites " A *Bacillus licheniformis* mutant host cell, said mutant host cell is derived from a parent *Bacillus licheniformis* which mutant host cell comprises a mutation in a gene encoding a polypeptide involved in antibiotic synthesis, wherein said gene is native to said host cell, and wherein said gene encodes a polypeptide which is at least 95% identical to the polypeptide of SEQ ID NO:2", because the claim recites "a gene that encodes a polypeptide involved in antibiotic synthesis" and also recites "said gene encodes a polypeptide which is at least 95% identical to SEQ ID NO:2" and it is unclear whether the polypeptide with the activity is the same as the polypeptide that has 95% identity to SEQ ID NO:2. Thus it is also unclear which of the recited polypeptides yields 5% less expression. Further the claim is unclear as to how the gene is mutated to produce said "mutated host cell". It is noted that claim 42 recites that said mutation occurs via deletion of a gene, however, independent claim 41 has to stand on its own. The dependent claims hereto are also included in this rejection.

Claim 42 is indefinite for the recitation of "a partial or complete deletion of said gene in claim 41", because how can a completely deleted gene express a polypeptide. Moreover, the instant specification discloses that the mutation is as a result of "...a partial or complete deletion of the one or more gene(s) encoding the one or more polypeptide(s) involved in antibiotic synthesis (see paragraph [0019]). Thus, it appears that several genes and polypeptides are involved in the antibiotic synthesis, which is only reflected in claim 43. Further, see also claim 59 for similar language.

Art Unit: 1652

Claim 50 is indefinite for the recitation of "an intermediate of interest", because it is unclear what constitutes an intermediate of interest, and no definition is provided in the specification.

Response to Arguments

9. The response filed has been considered. The rejections of record have been withdrawn based on applicant's amendments to the claims. Note that the rejections instituted under 35 U.S.C. 112, first paragraph are for different reasoning that previously of record, thus applicant's arguments are moot. The rejections herein are in place for the reasons stated above.

Conclusion

10. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax

Art Unit: 1652

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Primary Examiner

HOPE ROBINSON
PRIMARY EXAMINER

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: See Raw Sequence Listing Error Report

8. Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g).

For questions regarding compliance to these requirements, please contact:

- For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
- For CRF Submission Help, call (703) 308-4212
- For PatentIn software Program Support:
 - HELP DESK: (703) 739-8559, ext 508, M-F, 8 AM to 5 PM EST except holidays
 - Email: PATIN21HELP@uspto.gov
 - To purchase PatentIn software: (703) 306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE

Notice to Comply

08 OCT 2004

CRF Errors Edited by the STIC Systems Branch

Serial Number: 10/510,941

CRF Edit Date: 10-22-04
Edited by: KQ

☐ Realigned nucleic acid/amino acid numbers/text in cases where the sequence text "wrapped" to the next line

☐ Corrected the SEQ ID NO. Sequence numbers edited were:

☐ Inserted or corrected a nucleic number at the end of a nucleic line. SEQ ID NO's edited:

☒ Deleted: ☒ invalid beginning/end-of-file text ; _____ page numbers

☐ Inserted mandatory headings/numeric identifiers, specifically:

☐ Moved responses to same line as heading/numeric identifier, specifically:

☐ Other:

08 OCT 2004



PCT

RAW SEQUENCE LISTING

DATE: 10/22/2004

PATENT APPLICATION: US/10/510,941

TIME: 09:18:29

Input Set : A:\pto.kd.txt

Output Set: N:\CRF4\10222004\J510941.raw

```

3 <110> APPLICANT: Jorgensen, Steen Troels
4      Rasmussen, Michael Dolberg
5      Andersen, Jens Tonne
6      Olesen, Peter Bjarke
7      Clausen, Ib Groth
9 <120> TITLE OF INVENTION: Improved Bacillus Host Cell
11 <130> FILE REFERENCE: 10297.204-US
C--> 13 <140> CURRENT APPLICATION NUMBER: US/10/510,941
C--> 13 <141> CURRENT FILING DATE: 2004-10-08
13 <160> NUMBER OF SEQ ID NOS: 22
15 <170> SOFTWARE: PatentIn version 3.3
17 <210> SEQ ID NO: 1
18 <211> LENGTH: 1602
19 <212> TYPE: DNA
20 <213> ORGANISM: Bacillus licheniformis
23 <220> FEATURE:
24 <221> NAME/KEY: CDS
25 <222> LOCATION: (501)..(1421)
27 <400> SEQUENCE: 1
28 aacagccaga aaggagacga agaacgtctc tatttaacag agcttgatat gttctgcgtc      60
30 catttcgggt caaggatata ttcactatta tgaaaccaat ttttccgatt tccgtataaa      120
32 caaagcgtgg aacctgttaa aggacaagaa aaatcgacag ggaataaaaa atcggcaagc      180
34 ttcccaaagg gaaccggggc aggctgaagc tagcgctcac attggcgagc gatgcagcgg      240
36 tcgtgctgtt tgatgaacca tccggctctcc gatggtgagg gagtcgacag tcaaaagcct      300
38 tcttacatat ttggagcttg acaagcagac aatcgccatc gccacctatg aaattgaaca      360
40 aatattggat gtcgtcttaa atggccgaat tgaagcaaaa aaggatgtcg aacagctgcg      420
42 cgaggaatcc ggaatgtcgc ttttggaatg gctgaaacgg tttattaaag aaaaaaattg      480
44 aaaaagcggg aggagaaaca ttg gaa aca ctt ttg gaa tta aaa aat gta tca      533
45                                     Leu Glu Thr Leu Leu Glu Leu Lys Asn Val Ser
46                                     1           5           10
48 aaa acg atc agg ggg aaa aag atc atc gag ggc ttg agt ttt gac gtg      581
49 Lys Thr Ile Arg Gly Lys Lys Ile Ile Glu Gly Leu Ser Phe Asp Val
50                                     15           20           25
52 cgg gca ggc gag ata ttc ggc ttc ctg ggg ccg aac ggc gcc gga aaa      629
53 Arg Ala Gly Glu Ile Phe Gly Phe Leu Gly Pro Asn Gly Ala Gly Lys
54                                     30           35           40
56 acg acg acg atc cgg atg att gtc gga cat atg agc att acc gcc ggt      677
57 Thr Thr Thr Ile Arg Met Ile Val Gly His Met Ser Ile Thr Ala Gly
58                                     45           50           55
60 gaa atc gcc gtg tgc ggc gtc agc gta aaa gaa aac ttt gaa aag gct      725
61 Glu Ile Ala Val Cys Gly Val Ser Val Lys Glu Asn Phe Glu Lys Ala
62 60                                     65           70           75
64 gca cgg cat atc gga gcg atc gtt gaa aac ccg gag ctt tat aaa ttt      773

```


RAW SEQUENCE LISTING

DATE: 10/22/2004

PATENT APPLICATION: US/10/510,941

TIME: 09:18:29

Input Set : A:\pto.kd.txt

Output Set: N:\CRF4\10222004\J510941.raw

```

65 Ala Arg His Ile Gly Ala Ile Val Glu Asn Pro Glu Leu Tyr Lys Phe
66                               80                               85                               90
68 tta acg ggc tac caa aac ctt cag caa tac gcg cgc atg acg aaa ggc      821
69 Leu Thr Gly Tyr Gln Asn Leu Gln Gln Tyr Ala Arg Met Thr Lys Gly
70                               95                               100                               105
72 gtg acg aaa aag aaa att gac gaa atc gtc gag ctc gtc gga ttg aaa      869
73 Val Thr Lys Lys Lys Ile Asp Glu Ile Val Glu Leu Val Gly Leu Lys
74                               110                               115                               120
76 aac agg atc aac gac aag gtc aaa acg tat tcg tta gga atg aga caa      917
77 Asn Arg Ile Asn Asp Lys Val Lys Thr Tyr Ser Leu Gly Met Arg Gln
78                               125                               130                               135
80 agg ctt ggc ctt gcc caa agc ctt ttg cac gat cca aag ctg ttg att      965
81 Arg Leu Gly Leu Ala Gln Ser Leu Leu His Asp Pro Lys Leu Leu Ile
82 140                               145                               150                               155
84 ctc gat gag ccg acg aac ggg ctt gat ccg gca ggt atc cgg gaa atc      1013
85 Leu Asp Glu Pro Thr Asn Gly Leu Asp Pro Ala Gly Ile Arg Glu Ile
86                               160                               165                               170
88 cgt gac tat tta aga aag ctg acg aga gaa aag gga atg gcg gtc atc      1061
89 Arg Asp Tyr Leu Arg Lys Leu Thr Arg Glu Lys Gly Met Ala Val Ile
90                               175                               180                               185
92 gtt tca agc cac ctg ctt tca gaa atg gag ctg atg tgc gac agg atc      1109
93 Val Ser Ser His Leu Leu Ser Glu Met Glu Leu Met Cys Asp Arg Ile
94                               190                               195                               200
96 gcc att att caa aac gga aag ctc cgg gat att cag cat gtg cac gga      1157
97 Ala Ile Ile Gln Asn Gly Lys Leu Arg Asp Ile Gln His Val His Gly
98                               205                               210                               215
100 ccc gct cgg gat gag aag aag cgc tat tat att caa gcg gac gac acc      1205
101 Pro Ala Arg Asp Glu Lys Lys Arg Tyr Tyr Ile Gln Ala Asp Asp Thr
102 220                               225                               230                               235
104 cag gct ctc aca cgg gaa gcg gct gct ttc aga aag gtg aag gtt gac      1253
105 Gln Ala Leu Thr Arg Glu Ala Ala Ala Phe Arg Lys Val Lys Val Asp
106                               240                               245                               250
108 gaa gcg gaa ggc ggg ata gag ctc agc att caa aag gat gaa gtg cct      1301
109 Glu Ala Glu Gly Gly Ile Glu Leu Ser Ile Gln Lys Asp Glu Val Pro
110                               255                               260                               265
112 gat ttg att aaa cac ttg aca gac agc ggt gtt cgc tta tat gaa gtg      1349
113 Asp Leu Ile Lys His Leu Thr Asp Ser Gly Val Arg Leu Tyr Glu Val
114                               270                               275                               280
116 aag gct gtg aac aaa tcg ctg gaa gac cga ttc ctg gaa atc acc gca      1397
117 Lys Ala Val Asn Lys Ser Leu Glu Asp Arg Phe Leu Glu Ile Thr Ala
118                               285                               290                               295
120 gat aag gag gaa gct cag cat gtt taatctcatc gtaaataaat ggatcaaaat      1451
121 Asp Lys Glu Glu Ala Gln His Val
122 300                               305
124 ttttaatcga aaaggcacat acgtcatgat cggaattttg ctgttagctg tcatcgggct      1511
126 gggcgttctc acaaagacga tcggagagac agacaaaaac acggactgga aaaaggaatt      1571
128 ggcgcaggaa ataaggacaa gggggccttag t      1602
131 <210> SEQ ID NO: 2
132 <211> LENGTH: 307

```

RAW SEQUENCE LISTING

DATE: 10/22/2004

PATENT APPLICATION: US/10/510,941

TIME: 09:18:29

Input Set : A:\pto.kd.txt

Output Set: N:\CRF4\10222004\J510941.raw

```

133 <212> TYPE: PRT
134 <213> ORGANISM: Bacillus licheniformis
136 <400> SEQUENCE: 2
138 Leu Glu Thr Leu Leu Glu Leu Lys Asn Val Ser Lys Thr Ile Arg Gly
139 1 5 10 15
142 Lys Lys Ile Ile Glu Gly Leu Ser Phe Asp Val Arg Ala Gly Glu Ile
143 20 25 30
146 Phe Gly Phe Leu Gly Pro Asn Gly Ala Gly Lys Thr Thr Thr Ile Arg
147 35 40 45
150 Met Ile Val Gly His Met Ser Ile Thr Ala Gly Glu Ile Ala Val Cys
151 50 55 60
154 Gly Val Ser Val Lys Glu Asn Phe Glu Lys Ala Ala Arg His Ile Gly
155 65 70 75 80
158 Ala Ile Val Glu Asn Pro Glu Leu Tyr Lys Phe Leu Thr Gly Tyr Gln
159 85 90 95
162 Asn Leu Gln Gln Tyr Ala Arg Met Thr Lys Gly Val Thr Lys Lys Lys
163 100 105 110
166 Ile Asp Glu Ile Val Glu Leu Val Gly Leu Lys Asn Arg Ile Asn Asp
167 115 120 125
170 Lys Val Lys Thr Tyr Ser Leu Gly Met Arg Gln Arg Leu Gly Leu Ala
171 130 135 140
174 Gln Ser Leu Leu His Asp Pro Lys Leu Leu Ile Leu Asp Glu Pro Thr
175 145 150 155 160
178 Asn Gly Leu Asp Pro Ala Gly Ile Arg Glu Ile Arg Asp Tyr Leu Arg
179 165 170 175
182 Lys Leu Thr Arg Glu Lys Gly Met Ala Val Ile Val Ser Ser His Leu
183 180 185 190
186 Leu Ser Glu Met Glu Leu Met Cys Asp Arg Ile Ala Ile Ile Gln Asn
187 195 200 205
190 Gly Lys Leu Arg Asp Ile Gln His Val His Gly Pro Ala Arg Asp Glu
191 210 215 220
194 Lys Lys Arg Tyr Tyr Ile Gln Ala Asp Asp Thr Gln Ala Leu Thr Arg
195 225 230 235 240
198 Glu Ala Ala Ala Phe Arg Lys Val Lys Val Asp Glu Ala Glu Gly Gly
199 245 250 255
202 Ile Glu Leu Ser Ile Gln Lys Asp Glu Val Pro Asp Leu Ile Lys His
203 260 265 270
206 Leu Thr Asp Ser Gly Val Arg Leu Tyr Glu Val Lys Ala Val Asn Lys
207 275 280 285
210 Ser Leu Glu Asp Arg Phe Leu Glu Ile Thr Ala Asp Lys Glu Glu Ala
211 290 295 300
214 Gln His Val
215 305
218 <210> SEQ ID NO: 3
219 <211> LENGTH: 1938
220 <212> TYPE: DNA
221 <213> ORGANISM: Bacillus licheniformis
224 <220> FEATURE:
225 <221> NAME/KEY: CDS

```

RAW SEQUENCE LISTING

DATE: 10/22/2004

PATENT APPLICATION: US/10/510,941

TIME: 09:18:29

Input Set : A:\pto.kd.txt

Output Set: N:\CRF4\10222004\J510941.raw

```

226 <222> LOCATION: (501)..(1457)
228 <400> SEQUENCE: 3
229 cgcacgcggac ttttgaacgt cggaaccgaa gataaaaaag gaaatgagct tgccaagcag      60
231 acctttcaaaa aattgaagga aaccgatttg aatttcatcg gcaatgtgga agcccgcgat      120
233 atgctggacg gagtcgctga tgtcatcgctc acagacggct ttaccggtaa cgttgccttg      180
235 aaaacggtcg agggcgcggc gctgtccatt tttaaaatgc tgagaacgac gctgacttcg      240
237 agcttcacgg cgaagctcgc cgcttctgca ctgaagccga agctgaaaga aatgaaaacg      300
239 aaaatggatt actctgaata cggcggagcc ggattgttcg gcttaaaggc gcccgatcgc      360
241 aaagcgcacg gatcatctga cggacgcgcc gtttatcacg cgatccgcca ggccagagag      420
243 atggtcagcc aaaatgtcgc ggcatttctc gaagaaaaaa ttcaacaaaa agcagatgaa      480
245 tagtctggag gttttaacac atg ggc aag att gct ttt cta ttc ccg ggc caa      533
246                               Met Gly Lys Ile Ala Phe Leu Phe Pro Gly Gln
247                               1                               5                               10
249 ggt tcg cag cat atc ggc atg gga cac gaa ttg tat gaa aaa gaa ccg      581
250 Gly Ser Gln His Ile Gly Met Gly His Glu Leu Tyr Glu Lys Glu Pro
251                               15                               20                               25
253 aat gcg aag aag att ttt gaa gaa gcg gat caa acg ctt gaa aca aaa      629
254 Asn Ala Lys Lys Ile Phe Glu Glu Ala Asp Gln Thr Leu Glu Thr Lys
255                               30                               35                               40
257 ctg agc acc ctc atg ttt gaa ggg gat gca aag gaa ctg acg ctt aca      677
258 Leu Ser Thr Leu Met Phe Glu Gly Asp Ala Lys Glu Leu Thr Leu Thr
259                               45                               50                               55
261 tac aac gcg cag cca agc ctt tta acg gcg agc atc gca gcg ctt gaa      725
262 Tyr Asn Ala Gln Pro Ser Leu Leu Thr Ala Ser Ile Ala Ala Leu Glu
263 60                               65                               70                               75
265 aaa ctg aag gaa tac ggc att aaa gcc gac tat gcg gca ggt cac agc      773
266 Lys Leu Lys Glu Tyr Gly Ile Lys Ala Asp Tyr Ala Ala Gly His Ser
267                               80                               85                               90
269 ctc ggc gaa tac agc gca ttg gtc gct gcc ggc gcc ttg tcg ttt aaa      821
270 Leu Gly Glu Tyr Ser Ala Leu Val Ala Ala Gly Ala Leu Ser Phe Lys
271                               95                               100                               105
273 gat gcg gtt tat gcc gtc aga aag cgc ggc gaa ttc atg aat gaa gcc      869
274 Asp Ala Val Tyr Ala Val Arg Lys Arg Gly Glu Phe Met Asn Glu Ala
275                               110                               115                               120
277 gtg ccg gcg gga gaa ggc gcg atg gcg gcc att ctc ggc atg gac agc      917
278 Val Pro Ala Gly Glu Gly Ala Met Ala Ala Ile Leu Gly Met Asp Ser
279                               125                               130                               135
281 cag gcg ctg aaa gaa gtg acg gac aaa att tcc gaa gaa gga aac ctt      965
282 Gln Ala Leu Lys Glu Val Thr Asp Lys Ile Ser Glu Glu Gly Asn Leu
283 140                               145                               150                               155
285 gtt cag ctc gcc aat ttg aac tgc cct ggg caa atc gtc atc tcg gga      1013
286 Val Gln Leu Ala Asn Leu Asn Cys Pro Gly Gln Ile Val Ile Ser Gly
287                               160                               165                               170
289 aca gct aaa ggc gtg gag ctc gct tca gag ctt gcg aaa gaa aag ggc      1061
290 Thr Ala Lys Gly Val Glu Leu Ala Ser Glu Leu Ala Lys Glu Lys Gly
291                               175                               180                               185
293 gca aaa cgc gcg att cct ctc gaa gtc agc ggg ccg ttc cat tct gag      1109
294 Ala Lys Arg Ala Ile Pro Leu Glu Val Ser Gly Pro Phe His Ser Glu
295                               190                               195                               200

```

RAW SEQUENCE LISTING

DATE: 10/22/2004

PATENT APPLICATION: US/10/510,941

TIME: 09:18:29

Input Set : A:\pto.kd.txt

Output Set: N:\CRF4\10222004\J510941.raw

```

297 ctg atg aag ccg gca gct gat aag ctt cgt gaa gtt ctt gat gcg tgc      1157
298 Leu Met Lys Pro Ala Ala Asp Lys Leu Arg Glu Val Leu Asp Ala Cys
299      205                      210                      215
301 acg atc aac gac gca gcc att ccg gtc gtc tcc aac gta acg gcc gac      1205
302 Thr Ile Asn Asp Ala Ala Ile Pro Val Val Ser Asn Val Thr Ala Asp
303 220                      225                      230                      235
305 ttt gta acg gat aaa gac gac att aag aat aaa ctg att gaa cag ctg      1253
306 Phe Val Thr Asp Lys Asp Asp Ile Lys Asn Lys Leu Ile Glu Gln Leu
307      240                      245                      250
309 tat tcc cct gta cgc ttt gaa gaa aca atc agc cgc ctg att gac gaa      1301
310 Tyr Ser Pro Val Arg Phe Glu Glu Thr Ile Ser Arg Leu Ile Asp Glu
311      255                      260                      265
313 ggc gtc acg acc ttc att gaa atc ggt ccc gga aag gtt ttg tca ggg      1349
314 Gly Val Thr Thr Phe Ile Glu Ile Gly Pro Gly Lys Val Leu Ser Gly
315      270                      275                      280
317 ctt gtg aag aaa gtg aac cgc aga gtc aaa acg att gct gta tca gac      1397
318 Leu Val Lys Lys Val Asn Arg Arg Val Lys Thr Ile Ala Val Ser Asp
319      285                      290                      295
321 ccg aac aca att gaa ctt gcc gtt caa acg ttg aag gag gaa aac gaa      1445
322 Pro Asn Thr Ile Glu Leu Ala Val Gln Thr Leu Lys Glu Glu Asn Glu
323 300                      305                      310                      315
325 aat gct gga aaa taaaacagcc gttgtgacag gagcctcaag aggaatcggc      1497
326 Asn Ala Gly Lys
329 cgcgcgatcg ccctggacct ggcgaaaaac ggagcaaatg tcgtcgtcaa ctacgcggga      1557
331 aatgaagcga aagcgaacga agtcgtagac gaaatcaaag cgctcggccg cgatgcgttt      1617
333 gcttttaaaag cggacgtttc caatgcggat gaggttcagg cgatgatgaa ggaagcggtc      1677
335 ggacgcttcg gcacgcttga catccttgtc aacaatgcgg gcattactaa agacaatctg      1737
337 ttcatgagaa tgaaagaaga tgaatgggac gacgtcatta acataaaactt aaaaggtgtg      1797
339 ttcaattggt caaaagctgt gacaagacag atgatgaaac aaagaagcgg ccggatcatc      1857
341 aatatcacct cggttgtagg cgtcgtcggg aacgcggggc aggccaacta tgtcgcgggt      1917
343 aaatcaggcg tattccagta g                      1938
346 <210> SEQ ID NO: 4
347 <211> LENGTH: 319
348 <212> TYPE: PRT
349 <213> ORGANISM: Bacillus licheniformis
351 <400> SEQUENCE: 4
353 Met Gly Lys Ile Ala Phe Leu Phe Pro Gly Gln Gly Ser Gln His Ile
354 1      5      10      15
357 Gly Met Gly His Glu Leu Tyr Glu Lys Glu Pro Asn Ala Lys Lys Ile
358      20      25      30
361 Phe Glu Glu Ala Asp Gln Thr Leu Glu Thr Lys Leu Ser Thr Leu Met
362      35      40      45
365 Phe Glu Gly Asp Ala Lys Glu Leu Thr Leu Thr Tyr Asn Ala Gln Pro
366      50      55      60
369 Ser Leu Leu Thr Ala Ser Ile Ala Ala Leu Glu Lys Leu Lys Glu Tyr
370 65      70      75      80
373 Gly Ile Lys Ala Asp Tyr Ala Ala Gly His Ser Leu Gly Glu Tyr Ser
374      85      90      95
377 Ala Leu Val Ala Ala Gly Ala Leu Ser Phe Lys Asp Ala Val Tyr Ala

```

VERIFICATION SUMMARY

PATENT APPLICATION: US/10/510,941

DATE: 10/22/2004

TIME: 09:18:30

Input Set : A:\pto.kd.txt

Output Set: N:\CRF4\10222004\J510941.raw

L:13 M:270 C: Current Application Number differs, Replaced Current Application No

L:13 M:271 C: Current Filing Date differs, Replaced Current Filing Date